

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
15 April 2004 (15.04.2004)

PCT

(10) International Publication Number  
**WO 2004/031348 A3**

(51) International Patent Classification<sup>7</sup>: **A61B 5/055**  
(21) International Application Number:  
PCT/US2003/030155

(22) International Filing Date:  
24 September 2003 (24.09.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/413,673 24 September 2002 (24.09.2002) US

(71) Applicant (for all designated States except US): **THE GOVERNMENT OF THE UNITED STATES OF AMERICA** as represented by **THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; National Institutes of Health, Office of Technology Transfer, Suite 325, 6011 Executive Boulevard, Rockville, MD 20852-3804 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **OLDFIELD, Edward, H.** [US/US]; P.O. Box 309, Philomont, VA 22131 (US). **LONER, Russell, R.** [US/US]; 10611 Mantz Road, Silver Spring, MD 20903 (US). **GARMESTANI, Kayhan** [US/US]; 11208 Hurdle Hill Drive, Potomac, MD 20854 (US). **BRECHBIEL, Martin, W.** [US/US]; 3404 Monarch Lane, Annandale, VA 22003-1155 (US).

(74) Agent: **NOONAN, William, D.**; Klarquist Sparkman, LLP, One World Trade Center, Suite 1600, 121 SW Salmon Street, Portland, OR 97204 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
15 July 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR CONVECTION ENHANCED DELIVERY OF THERAPEUTIC AGENTS

(57) Abstract: A method for monitoring and controlling convection enhanced delivery of a therapeutic agent to a target tissue is disclosed. A tracer that is detectable, for example, by magnetic resonance imaging (MRI) and/or by X-ray computed tomography (CT) is co-infused with the therapeutic agent and used to monitor the distribution of the therapeutic agent as it moves through the target tissue. The images obtained during delivery are used to confirm delivery of the therapeutic agent to the target tissue and to avoid exposure of tissue outside of the targeted area to the therapeutic agent. In addition, the signal intensity of the images may be used to confirm that the therapeutic agent has been delivered to the target tissue at a desired concentration.

WO 2004/031348 A3

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/30155

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61B 5/055

US CL : 424/9.3

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/9.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
EAST; Dialog

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LONSER, R.R. et al. Direct convective delivery of macromolecules to the spinal cord. J. Neurosurg. October, 1998. Vol. 89, pages 616-622, see entire document.	1-36

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z"

document member of the same patent family

Date of the actual completion of the international search

23 February 2004 (23.02.2004)

Date of mailing of the international search report

27 MAY 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Karen Cochrane Carlson, Ph.D.

Telephone No. 703-308-1235

Form PCT/ISA/210 (second sheet) (July 1998)

Best Available Copy